Docket No.: UMY-038
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Zuoshang Xu *et al.*

Application No.: 10/700,816 Confirmation No.: 9864

Filed: November 4, 2003 Art Unit: 1635

For: ALLELE-SPECIFIC RNA INTERFERENCE Examiner: S. McGarry

DECLARATION UNDER 37 C.F.R. §1.131

We, Zuoshang Xu and Phillip D. Zamore, state and declare the following:

1. We are co-inventors of the above-identified patent application.

2. This Declaration is submitted as evidence that the subject matter claimed in the above-identified application was invented prior to August 5, 2002.

3. We jointly submitted a grant application entitled "RNAi as a Potential Therapy for Amyotrophic Lateral Sclerosis" prior to August 5, 2002.

4. Data included in our grant application is enclosed herewith as Exhibit A. Exhibit A depicts the results of an *in vitro* RNAi experiment in which siRNAs[1] complementary to either mutant or wild-type SOD1 allele were added to a Drosophila embryo extract containing full-length, radiolabelled mutant or wild type SOD1 mRNA. mRNA cleavage was assessed by a cleavage assay. The data in Exhibit A demonstrate that siRNA duplexes can discriminate between mutant and wild-type alleles *in vitro*.

5. Data generated by us following submission of our grant application and prior to August 5, 2002 is included herewith as Exhibit B. Exhibit B depicts the result of an experiment in which human cells were transfected with (1) a plasmid encoding either a wild-type SOD1:GFP fusion protein or a mutant SOD1 G85R:GFP fusion protein; and (2) an siRNA complementary to either the wild-type or mutant G85R allele of SOD1. Expression of either mutant or wild-type SOD1 was measured by FACS analysis. The data in Exhibit B demonstrate that siRNA duplexes can discriminate between mutant and wild-type alleles in human cells.

[1] We note that certain of the siRNAs are mislabeled in panel A of Exhibit A. Mutant siRNAs P9 and P11 should be mutant siRNAs P11 and P9, respectively. Wild-type siRNAs P11 and P9 should be wild-type siRNAs P9 and P11, respectively.

6. Thus, the above-identified data demonstrates that we had successfully reduced to practice a method for conducting allele-specific RNA interference of a target allele.

7. The above-identified data accurately describes the invention we made prior to August 5, 2002 and provides support for the claims as originally filed in the above-identified application.

8. Accordingly, this Declaration establishes a date of invention for the above-identified application at least as early as August 5, 2002.

We, the undersigned, declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

Dr. Zuoshang Xu — Date: 9/11/2007

Dr. Phillip D. Zamore — Date: 9/11/2007

Exhibit A

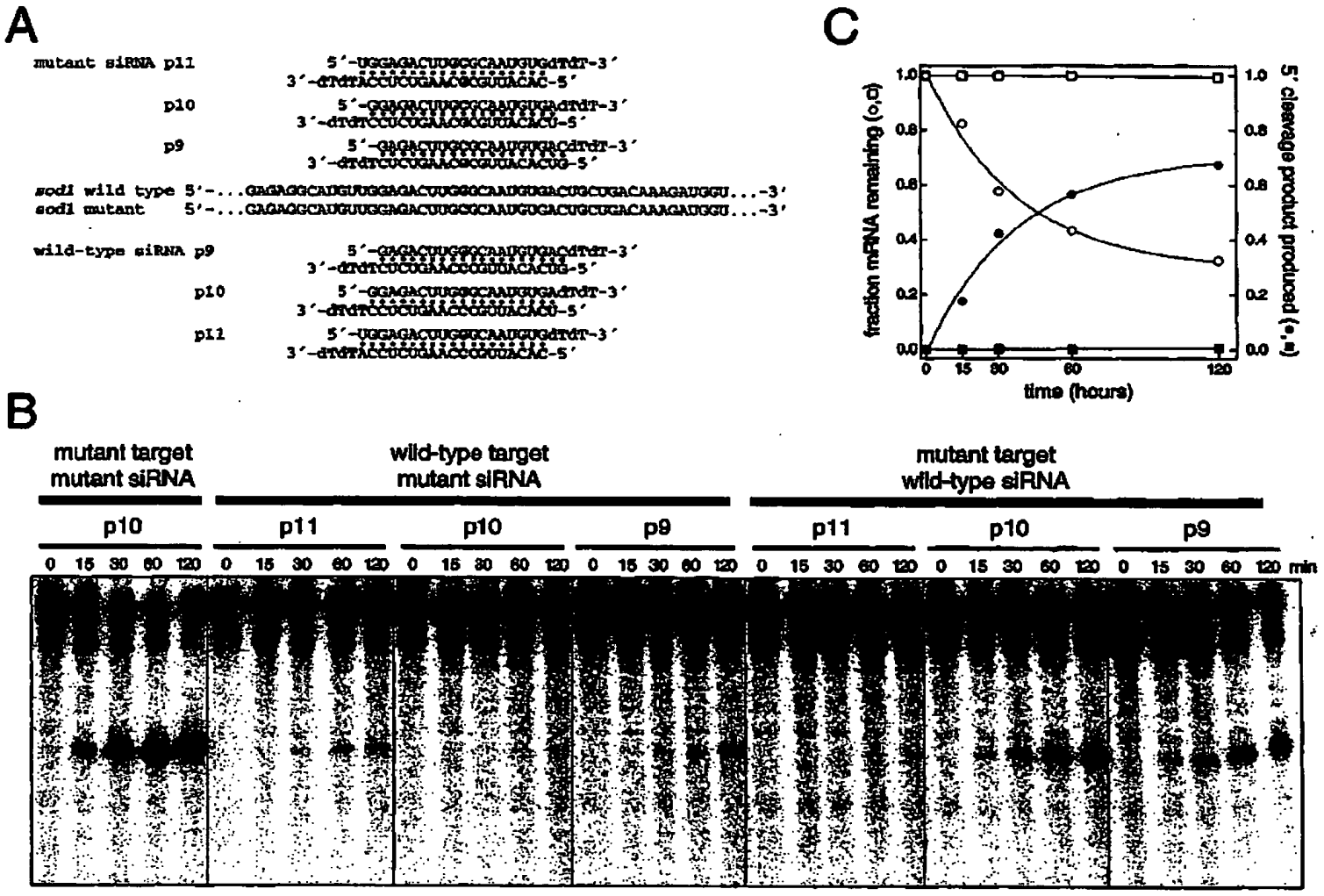
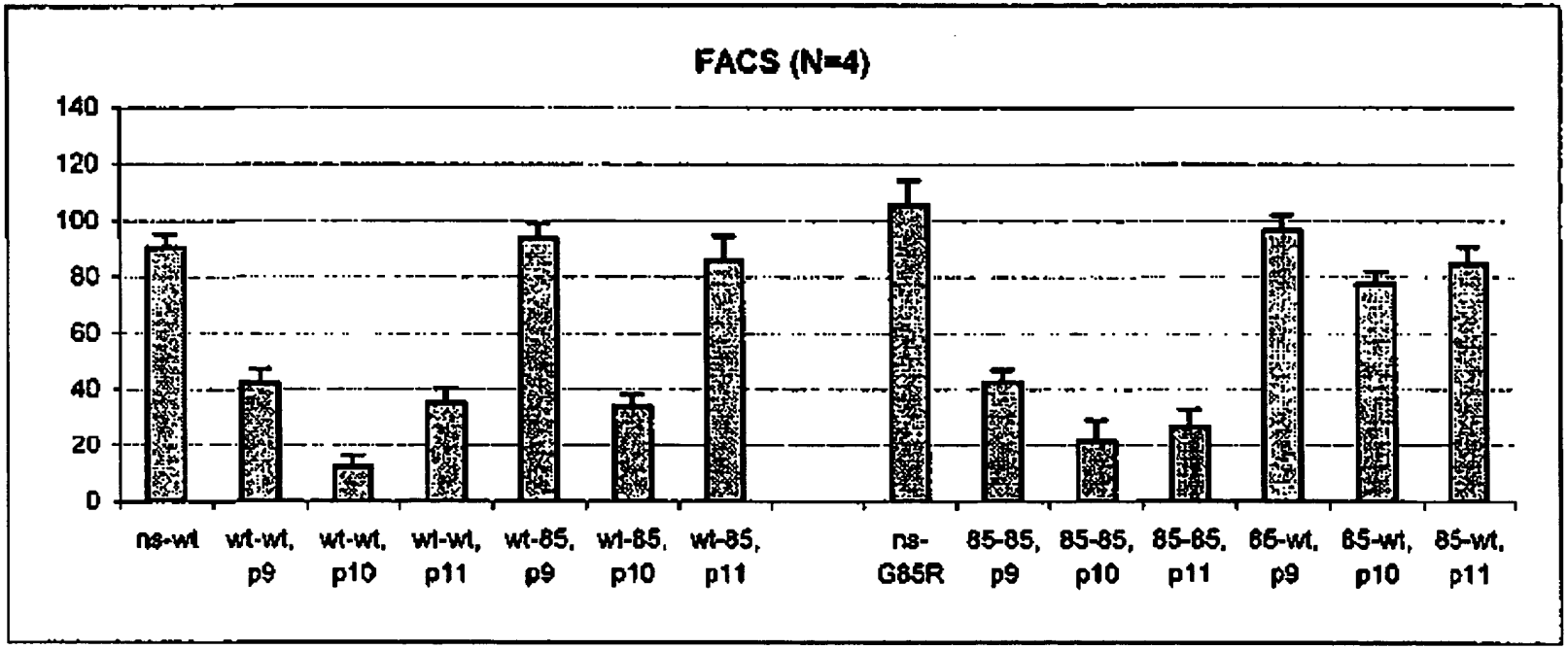


Figure 2. siRNA duplexes can discriminate between mutant and wild-type SOD1 in vitro. (A) siRNA duplexes used. (B) In vitro RNAi experiments targeting mutant or wild-type SOD1 mRNA with mutant or wild-type siRNAs. (C) Mutant siRNA p10 targets mutant but not wild-type SOD1 mRNA for destruction by the RNAi pathway.

Exhibit B


FACS (N=4)
140
120
100
80
60
40
20
0
ns-wt
wt-wt, p9
wt-wt, p10
wt-wt, p11
wt-85, p9
wt-85, p10
wt-85, p11
ns-G85R
85-85, p9
85-85, p10
85-85, p11
85-wt, p9
85-wt, p10
85-wt, p11